

## Synthesis, Spectroscopic Characterization, Electrochemical and Antimicrobial Studies of Copper(II), Nickel(II), Cobalt(II) and Zinc(II) Complexes Derived from 1-Phenyl-2,3-dimethyl-4(2-iminomethylbenzylidene)-pyroazol-5-( $\alpha$ -imino)-indole-3-propionic Acid<sup>†</sup>

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**Abstract:** Neutral tridentate N<sub>2</sub>O complexes of Cu(II), Ni(II), Co(II) and Zn(II) have been synthesized using the 1-phenyl-2,3-dimethyl-4(2-iminomethylbenzylidene)-pyroazol-5-( $\alpha$ -imino)-indole-3-propionic acid (H<sub>2</sub>L). All the complexes were characterized by elemental analysis, molar conductivity, magnetic susceptibility data, IR, <sup>1</sup>H-NMR, UV-Vis, FAB-Mass and EPR spectral studies. The physicochemical studies and spectral data indicate that the ligand acts as a divalent tridentate chelating agent. All the complexes have the general composition [ML<sub>2</sub>] (M= Cu(II), Ni(II), Co(II) and Zn(II); L = Schiff base). The IR, UV-Vis., magnetic susceptibility measurements and EPR spectral data of the complexes suggest that all the complexes are octahedral geometry. The lower conductivity data confirm the non-electrolytic nature of the complexes. The effect of redox potential on Cu(II) and Ni(II) ions by the ligand environment is studied by cyclic voltammetric measurements. The Schiff base and its metal complexes were utilized to test the *in vitro* antimicrobial activities, which gave good results in the presence of metal ion than the free ligand environment against the different species of microorganisms.

**Keywords:** Synthesis, Cyclic Voltammetric measurements, Neutral tridentate N<sub>2</sub>O complexes

### Introduction

The transition metal complexes of 4-aminoantipyrine and its complexes have been extensively examined due to their wide applications in various fields like biological, pharmacological, clinical, analytical and industrial area. A search through the literature reveals that no work has been done on the transition metal complexes of Schiff bases formed by the condensation of acetophenylidene-4-aminoantipyrine with tryptophan<sup>1-14</sup>. We report

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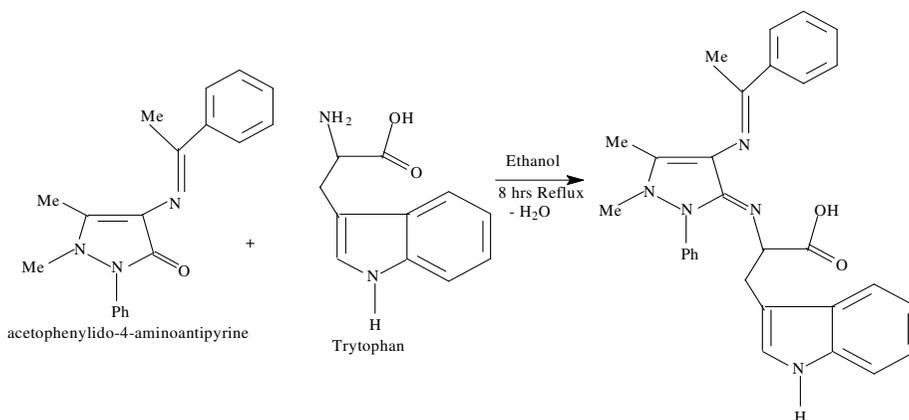
herein the synthesis, characterization, redox and antimicrobial studies of transition metal complexes containing Schiff base derived from acetophenylidene-4-aminoantipyrine and tryptophan. The synthesized compounds are NNO donor type and its ligation behavior with different metal ions was studied.

## Experimental

All the reagents, 4-aminoantipyrine, acetophenone, tryptophan and the metal salts were purchased from Merck. Melting points of ligands and complexes were determined on electrochemical capillary apparatus. Elemental analysis was obtained by using a thermal finger-flash CA, 112 series at sophisticated analytical instrumentation facility, IIT, Mumbai. The IR spectra of the samples were recorded on a FT-IR Shimadzu model (8400S) in a KBr pellets and electronic spectra in acetonitrile were recorded using Shimadzu model (1800) spectrophotometer. Conductivity measurements were carried out at room temperature on freshly prepared  $10^{-3}$  M acetonitrile solution was measured using a 305 model systronic conductivity bridge with a dip type cell.  $^1\text{H}$  NMR spectra of the Schiff base and its zinc complex were recorded in  $\text{CDCl}_3$  solution on a Bruker 300 MHz FT-NMR spectrometer using TMS as internal standard at Madurai Kamaraj University, Madurai. Cyclic voltammogram of the complexes was recorded in MeCN solution at 300 K using BAS CV 50 electrochemical analyzer. CV measurements were performed using a glassy carbon working electrode, platinum wire auxiliary electrode and an Ag/AgCl reference electrode. Tetrabutyl ammonium bromide was used as supporting electrolyte. The X-band ESR spectra of the copper and vanadyl complexes in MeCN solution at 300 K and 77 K using TCNE (Tetracyanoethylene) as the  $g$ -marker were recorded on a Varian E-112 ESR spectrometer at Sophisticated Analytical Instrumentation facility, IIT, Mumbai. Magnetic susceptibility of the complexes was measured by Guoy balance using copper sulphate as calibrant. The antimicrobial activities of the ligand and their complexes were carried out by disc diffusion method.

### Synthesis of Schiff base ( $\text{H}_2\text{L}$ )

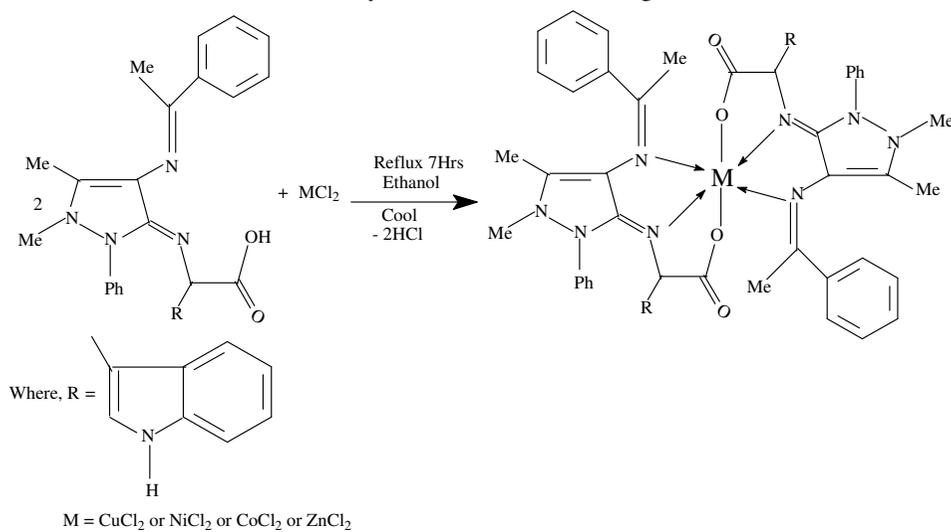
An ethanolic solution (50 mL) of acetophenylidene-4-aminoantipyrine (3.05 g, 0.01 mol) and tryptophan (2.04 g, 0.01 mol) was boiled under reflux on a water bath for 8 h. Then the resulting solution was concentrated to 10 mL and stirred with 5 mL of (30%) ammonia solution. The solid obtained was collected by filtration and recrystallised from ethanol. The scheme for the synthesis of Schiff base is given below:



Scheme 1

### Synthesis of complexes

An ethanolic solution of  $\text{CuCl}_2/\text{NiCl}_2/\text{CoCl}_2/\text{ZnCl}_2$  (0.05 mol) and Schiff base (0.05 mol) was stirred for 7 h and then concentrated to 10 mL. The mixture was cooled at room temperature for 12 h and the precipitated complexes was filtered, washed with ethanol and dried. The reaction scheme for the synthesis of Schiff base is given below:



**Scheme 2**

### Procedure for antimicrobial activity

*In vitro* antibacterial and antifungal activity assay was performed by disc diffusion method using nutrient agar as the medium. The Schiff base and its metal complexes were tested against bacteria (*Escherichia coli*, *Salmonella typhi*, *Staphylococcus aureus*, *Staphylococci* and *Pseudomonas aeruginosa*) and fungi (*Candida albicans*). The stock solutions were prepared by dissolving the compounds in MeCN and the solutions are serially diluted in order to find the minimum inhibitory concentration values (MIC). All the blank discs were moistened with the solvent. For disc assays, the compounds containing disc (6 mm) with various concentrations were placed on the surface of the nutrient agar plate previously spread with 0.1 mL of overnight culture of microorganisms. Then, the plates were incubated at 37 °C for 48 h. During this period, the test solution was diffused and affected the growth of the microorganisms. Hence, the inhibition zones were developed on the plate around the disc. The concentration at which the zone developed was noted as MIC value of the synthesized compounds.

### Results and Discussion

The analytical data of the complexes correspond well with the general formula  $\text{ML}_2$ . Their magnetic susceptibilities at room temperature are consistent with octahedral geometry around the central metal ion. The low conductance of the chelates supports their non-electrolytic nature<sup>15</sup>.

### Mass spectra

The mass spectra of the ligand and its copper complex were recorded and compared for their stoichiometric composition. The molecular ion peak for the ligand was observed at 491  $m/z$  ratio ( $\text{C}_{30}\text{H}_{29}\text{O}_2\text{N}_5$ ). For copper complex, the molecular ion peak appeared at 1044  $m/z$  ( $\text{CuC}_{60}\text{H}_{56}\text{O}_4\text{N}_{10}$ ) which confirms the stoichiometry of metal complexes as being of the  $\text{ML}_2$  type.

**Table 1.** Physical characterization, analytical, molar conductance and magnetic susceptibility data of the Schiff base and its complexes

Compd	Colour	M.P./Decomp Point, °C	Found (Calcd), %				$\Lambda_M \times 10^{-3}$ mho cm <sup>2</sup> mol <sup>-1</sup>	$\mu_{\text{eff.}}$ (B.M.)
			M	C	H	N		
HL	Red	126	-	73.36 (73.32)	5.83 (5.91)	14.68 (14.26)	-	-
[CuL]	brown	202	5.96 (6.09)	68.85 (69.00)	5.17 (5.37)	13.92 (13.42)	1.89	1.77
[NiL]	green	178	5.13 (5.65)	68.94 (69.32)	5.21 (5.39)	13.56 (13.48)	2.01	-
[CoL]	Red	196	5.59 (5.67)	69.12 (69.30)	5.11 (5.39)	13.06 (13.48)	1.55	3.89
[ZnL]	brown	226	6.28 (6.01)	68.14 (68.85)	5.18 (5.36)	13.62 (13.39)	2.35	-

### IR spectra

The IR spectrum of the ligand shows a strong broad band at 3500- 3300 cm<sup>-1</sup> region which are assigned to -COOH group of tryptophan moiety. Disappearance of this band indicates the deprotonation of this group upon coordination. IR spectra of all complexes shows a new strong band at 3150 cm<sup>-1</sup> region which are assigned to cyclic -NH- group of tryptophan moiety and the same peak is also appeared in the IR spectrum of ligand as a weak node due to merging of -OH groups. It indicates that there is a free existence of this group and not involved in coordination with metal ion. In the spectrum of the Schiff base, the strong bands at 1615 - 1600 cm<sup>-1</sup> region are attributable to -C=N groups. On chelation, due the possible drift of lone pair electron density towards the metal ion, the azomethine -C=N band is expected to absorb at lower frequency in the complex. The observed band at 1595 - 1580 cm<sup>-1</sup> region indicates the coordination of azomethine nitrogen to the metal. Moreover, the Schiff base and all the complexes exhibit an intense peak at 1665 cm<sup>-1</sup>, a characteristic feature of the -C=O stretching frequency indicating the existence of -C=O of acid group in tryptophen moiety. IR spectra of the complexes also show a new peaks at 510 cm<sup>-1</sup> and 430 cm<sup>-1</sup> region due to the formation of M-N and M-O bond respectively<sup>16</sup>.

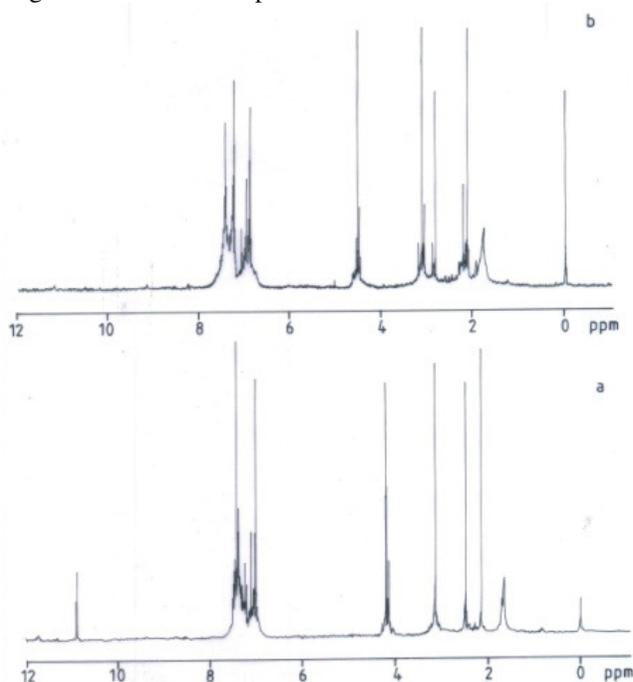
### Electronic absorption spectra

The ligand in MeCN shows a absorption band at 220 nm. The UV-Vis. spectrum of copper complex in MeCN shows two bands which are assigned as an intraligand charge transfer band (242 nm) and a d-d band (<sup>2</sup>E<sub>g</sub> → <sup>2</sup>T<sub>2g</sub>), (635 nm). The d-d band strongly favours octahedral geometry around the metal ion. The nickel complex in MeCN shows three d-d bands at 527 nm, 635 nm and 708 nm which are assigned as <sup>3</sup>A<sub>2g</sub>(F) → <sup>3</sup>T<sub>2g</sub>(F), <sup>3</sup>A<sub>2g</sub>(F) → <sup>3</sup>T<sub>1g</sub>(F) and <sup>3</sup>A<sub>2g</sub>(F) → <sup>3</sup>T<sub>1g</sub>(P) transitions respectively. The appearance of a band in the near IR region (708 nm) is characteristic for octahedral geometry. The cobalt complex in MeCN shows three bands at 510 nm, 642 nm and 894 nm which are assigned as <sup>4</sup>T<sub>1g</sub>(F) → <sup>4</sup>T<sub>2g</sub>(F), <sup>4</sup>T<sub>1g</sub>(F) → <sup>4</sup>A<sub>2g</sub>(F) and <sup>4</sup>T<sub>1g</sub>(F) → <sup>4</sup>T<sub>1g</sub>(P) transitions respectively. This complex also shows a characteristic band at 894 which conforms the octahedral coordination<sup>17,18</sup>.

### <sup>1</sup>H NMR spectra

<sup>1</sup>H NMR spectra of the Schiff base (H<sub>2</sub>L) and its zinc complex (Figure 1) were recorded in CDCl<sub>3</sub>. The Schiff base shows a peak at 10.84 ppm which is attributable to the -COOH

group of tryptophan moiety. Absence of this peak in the zinc complex which favours the loss of  $-\text{COOH}$  proton due to coordination with zinc ion. A slight down field shift was noted in all other signals in the zinc complex.



**Figure 1.**  $^1\text{H}$  NMR spectra of the Schiff base (a) and its zinc (b) complex in  $\text{CDCl}_3$  solution

### *Electrochemical behavior*

Cyclic voltammetry helps to evaluate the effect of ligands on the redox potential of the central metal ion in complexes. Cyclic voltammetry has been shown to be a particularly useful technique in studies of this type, aiding one to measure the existence of short lived species, as well as to study the ligand's structural parameters such as size and degree of conjugation. Cyclic voltammogram of the Cu(II) and Ni(II) complexes were recorded in MeCN solution using  $\text{LiClO}_4$  as supporting electrolyte and the values are summarized in Table 2.

**Table 2.** Redox potential for the Cu(II) and Ni(II) complexes in MeCN solution containing 0.1 M  $\text{LiClO}_4$  at 300 K at scan rate  $100 \text{ mVs}^{-1}$

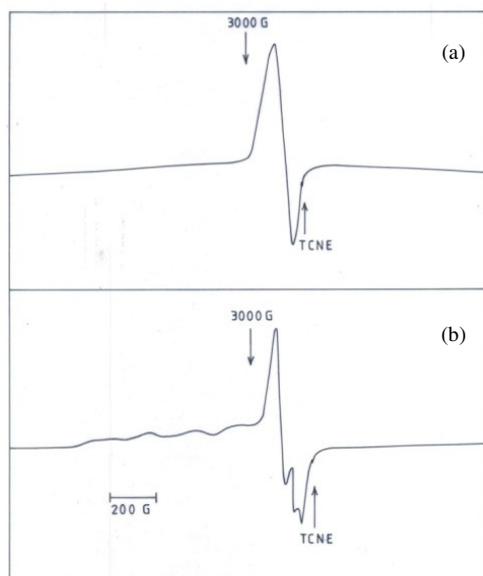
Complex	Couple	$E_{p_a}$ , V	$E_{p_c}$ , V	$I_{p_a}$ , $\mu\text{A}$	$I_{p_c}$ , $\mu\text{A}$
[CuL <sub>2</sub> ]	Cu(II)/Cu(III)	0.67	0.35	- 27	29
	Cu(II)/Cu(I)	-0.46	-0.59	- 41	32
[NiL <sub>2</sub> ]	Ni(II)/Ni(III)	0.76	0.49	- 46	35
	Ni(II)/Ni(I)	-0.57	- 0.73	- 52	47

The cyclic voltammogram of the copper complex in MeCN solution shows a reversible peak for the couple:  $\text{Cu(II)} \rightarrow \text{Cu(III)}$  at  $E_{p_a} = 0.67 \text{ V}$  with the direct cathodic peak for  $\text{Cu(III)} \rightarrow \text{Cu(II)}$  at  $E_{p_c} = 0.35 \text{ V}$ . Further, it exhibits another one couple characteristics for  $\text{Cu(II)} \rightarrow \text{Cu(I)}$  ( $E_{p_c} = -0.59 \text{ V}$ ) reduction and  $\text{Cu(I)} \rightarrow \text{Cu(II)}$  ( $E_{p_a} = -0.46 \text{ V}$ ) oxidation. The one-electron transfer process is established by the comparison of  $I_{p_c}$  and  $I_{p_a}$  values<sup>19</sup>.

The cyclic voltammogram of the nickel complex in MeCN solution shows a well defined redox process corresponding to the formation of the Ni(II)/Ni(III) couple at  $E_{p_a} = 0.76$  V and the associated cathodic peak observed at  $E_{p_c} = 0.59$  V. This couple is found to be quasi reversible and the ratio of anodic to cathodic peak currents ( $I_{p_c}/I_{p_a} = 0.93$ ) is corresponding to simple one-electron process. This complex also shows another quasi reversible peak in the negative region characteristics for Ni(II)  $\rightarrow$  Ni(I) reduction at  $E_{p_c} = -0.73$  V with the associated anodic peak at  $E_{p_a} = -0.57$  V for Ni(I)  $\rightarrow$  Ni(II) oxidation.

### ESR spectra

The ESR spectra of the copper complex, recorded in MeCN solution at 300 K and 77 K are shown in Figure 2.



**Figure 2.** ESR spectra of copper complex in MeCN at (a) 300K and (b) 77K

The spin Hamiltonian parameters for the copper complex are calculated from the spectra. The observed order ( $A_{||} = 156 > A_{\perp} = 70$ ;  $g_{||} = 2.37 > g_{\perp} = 2.09$ ) indicates that the complex is akin to axially elongated octahedral geometry. Further, it is also supported from the fact that the unpaired electron lies predominantly in the  $d_{x^2-y^2}$  orbital. Furthermore, Massacesiet *al.* reported that  $g_{||}$  is 2.4 for copper-oxygen bonds, 2.3 for copper-nitrogen bonds. For mixed copper-nitrogen and copper-oxygen system, there is a small variation in the point symmetry from octahedral geometry<sup>20</sup>.

For the copper complex  $g_{||} = 2.37$  which is in between 2.3 - 2.4. It shows that it is having mixed copper-nitrogen and copper-oxygen bonds in these chelate. Furthermore, this conclusion is also supported by the fact that the unpaired electron lies predominantly in the  $dx^2-y^2$  orbital, as was evident from the value of the term  $G$ , estimated from the expression<sup>21,22</sup>:

$$G = g_{||} - 2.0023/g_{\perp} - 2.0023$$

If  $G > 4$ , the local tetragonal axes are aligned parallel or only slightly misaligned. The observed value for the exchange interaction parameter for the complex is 4.1 suggest that the

local tetragonal axes are aligned parallel or slightly misaligned and the unpaired electron is present in the  $dx^2-y^2$  orbital. The observed value of  $\alpha^2$  (0.87) indicates that complex have some covalent character. The observed  $\beta^2$  (1.00) and  $\gamma^2$  (0.96) values indicate that there is no substantial interaction in the out-of-plane  $\pi$ -bonding and in-plane  $\pi$ -bonding which are completely ionic.

### Biological activities

The *in-vitro* biological screening effects of the investigated compounds were tested against the bacteria and fungi by disc diffusion method using nutrients agar as the medium and the data were summarized in Table 3.

**Table 3.** Antimicrobial activity of the Schiff base and its complexes (MIC in mg)

Compd	<i>Escherichia coli</i>	<i>Salmonella typhi</i>	<i>Pseudomonas aeruginosa</i>	<i>Staphylococcus aureus</i>	<i>Starptococci</i>	<i>Candida albicans</i>
HL	75	70	70	60	100	110
[CuL <sub>2</sub> ]	65	60	60	45	80	100
[NiL <sub>2</sub> ]	70	70	70	75	85	95
[CoL <sub>2</sub> ]	65	65	65	55	80	90
[ZnL <sub>2</sub> ]	55	45	55	50	60	65

From the table, it is clear that the zone of inhibition area is much larger for metal chelates than the ligand. Such increased activity of the metal chelates can be explained on the basis of chelation theory. On chelation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital. Further, it increases the delocalization of  $\pi$ -electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity leads to break-down of the permeability barrier of the cell and thus retards the normal cell processes<sup>23-26</sup>.

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